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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,842	07/05/2000	KAZUYUKI SUGIYAMA	Q60017	2682

7590

06/03/2002

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EXAMINER

DO, PENSEE T

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 06/03/2002

6

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/582,842

Applicant(s)

SUGIYAMA ET AL.

Examiner

Pensee T. Do

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3, 6-12 and 24-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-12, 24-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

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## **DETAILED ACTION**

### **Amendment Entry**

The amendment filed on March 4, 2002 has been acknowledged and entered.

Claims 4, 5, 13-23 are canceled. New claims 24-30 are added. Claims 1-3, 6-12, 24-30 are pending.

### ***Withdrawn Objections & Rejections***

Objection under 37 C.F.R. 1.75(c) is withdrawn herein.

Rejections under 35 USC 112, 2<sup>nd</sup> paragraph, 102 and 103 are withdrawn herein.

### ***Response to Arguments***

Applicant's arguments with respect to claim 1-3, 6-12, 24-30 have been considered but are moot in view of the new ground(s) of rejection.

## **NEW GROUNDS OF REJECTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-12, 24-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For all claims, "capable of" is indefinite because it is unclear of how the biotinylated binding component is modified to be capable of binding the compound.

For claims 1, 2, 6-12, 24-30, "crosslinked avidin" is unclear because such term would be interpreted in many ways such as many avidins crosslinked together since biotin binds to the avidin naturally without the aid of a crosslinker or that the avidin is bound to a linker which links the avidin and the biotin together.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme-biotin acceptor fused protein, does not reasonably provide enablement for a biotinylated fused-protein of an enzyme and a biotin acceptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification describes on page 3 that when a gene containing a luciferase gene and a cell, a biotin acceptor gene ligated thereto is expressed in a host cell, a luciferase-biotin acceptor fused protein is synthesized in a host cell. The specification does not teach that the biotinylated enzyme is a biotinylated fused protein of an enzyme and a biotin acceptor for biotin acceptor has many different meanings such as an avidin which can bind to biotin.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 6, 7-9, 12, 24, 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haughland et al. (US 5,443,986) further in view of Giese (US 4,478,914).

Haughland teaches a biotin-avidin-biotin complex comprising two biotin-introduced products which are the same or different (see table 12 in col. 22); and a avidin sandwiched therebetween (see col. 22, table 12) wherein at least one of the two biotin-introduced products is labeled and the other one is a biotin-introduced binding component (see col. 22). Haughland also teaches an enzyme-mediated technique such as enzyme-linked immunosorbent assay (ELISA) to detect analytes (see col. 22, lines 4-51). The method of the assay comprises combining the biotin-introduced enzyme, the sample containing analyte, and the biotin-binding component, an avidin to connect the two biotins together. The signal of the enzyme is detected. The binding component is a DNA (see col. 22, table 12). The biotin-introduced labeling substance is a biotin-introduced enzyme (see col. 22, table 12). Kits containing reagents for carrying out the methods are also disclosed in Haughland (see col. 40, example 19).

However, Haughland fails to teach a cross-linked avidin.

Giese teaches a process comprises of applying alternate successive layers of a first or second materials to a surface to be modified. The first material comprises a ligand binding proteinaceous material and the second material comprises a reactive ligand extender material, wherein the proteinaceous first material is selected from the

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group consisting of lectins, protein A, avidin derivatives including a crosslinked avidin, streptavidin, antibodies and combinations thereof, the second material is selected from biotin, biotin derivatives, biotin analogs, Fc fragments, hapten and combinations thereof. Avidin is a protein found in egg whites. (see col. 1, lines 15-20; line 50-col. 4, line 62).

It would have been obvious to one of ordinary skill in the art to use the crosslinked avidin of Giese in the method of Haughland since Giese's end product would have layers of biotin-avidin-biotin on a solid support. Furthermore, the crosslinked avidin is more stable and has high biotin affinity than the non-crosslinked avidin and thus the complex of biotin-crosslinked avidin-biotin would be more stable. An increase in affinity and stability between the avidin and the biotin would be an advantage in reduced product storage. Assays and kits comprising increased affinity avidin, because of the additional stability, have a longer shelf and less fastidious in shipping and storage requirements. The enhanced stability of these assays and kits would reduce the cost to the consumer. Regarding claim 8, since Giese teaches that the second material is a biotin or biotin derivatives, Fc fragments, and combinations thereof, it would have been obvious to one of ordinary skills in the art to combine biotin and Fc fragments to detect antigen since antibody fragment such as Fc fragment efficiently binds to the antigen more specifically with high affinity.

Claims 10, 11, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haughland et al. (US 5,443,986) and Giese further in view of Tatsumi (US 5,843,746).

Haughland et al. and Giese have been discussed above.

However, Haughland and Giese fail to teach a biotin-introduced fused-protein of an enzyme such as a biotin-introduced luciferase.

Tatsumi teaches a fusion protein (biotinated firely luciferase) which can be applied to a variety of bioluminescent analysis methods. For example, the biotinated firely luciferase can be bound through the biotin thereof to avidin or streptavidin to form a luciferase complex and a luminescent analysis method using such a firely luciferase complex can be applied to a detection system using biotin-avidin in techniques such as enzyme immunoassays, DNA probe method, immunostaining, receptor measurement, in situ hybridization, etc. (see col. 3, lines 33-41; col. 4, lines 25-35). Tatsumi also teaches using goat anti-mouse IgG Fc fragment-specific polyclonal antibody in the method of detecting for the enzyme activity. (see col. 7, lines 40-55).

It would have been obvious to one of ordinary skill in the art to use the fused protein of Tatsumi in the combined method of Haughland and Giese for detecting the activity of luciferase since Haughland teaches an enzyme immunoassay method of using binding agent-biotin-avidin-biotin-enzyme and the enzyme luciferase of Tatsumi can be biotinylated. Since the biotinated firely luciferase of Tatsumi yields a much higher percentage of activity upon binding to streptavidin compared to that of a chemically modified biotinated firely luciferase, e.g. 93% to 62% respectively. Furthermore, the biotinated firely luciferase of Tatsumi attains 10 times sensitivity as high as the conventional chemically modified biotinated firely luciferase. With respect to the fragment Fab', since it depends on the analyte being detected, one of ordinary skill

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in the art would find it obvious to use fragment Fab's in the detection of antigen since fragment Fab' provides specificity

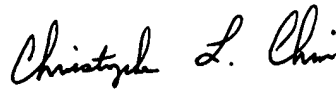
**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 703-308-4398. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-746-5291 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Pensee T. Do  
Patent Examiner  
May 30, 2002

  
CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1800/1641